New gene variant discovered for ALS

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(Medical Xpress)—Research led by King's College London has identified a new genetic variant, located on chromosome 17, associated with sporadic amyotrophic lateral sclerosis (ALS) – the most common form of motor neurone disease (MND).

With genetic data from over 17,000 individuals, the study is the largest of its kind and provides a new insight into the genetic structure of the disease.

ALS is a neurodegenerative disease which causes progressive muscle paralysis and is fatal within 3-5 years. Around 10 per cent of cases run in families, with the remainder occurring sporadically. Previous studies have identified a number of genetic variants associated with familial ALS, but for non-familial, or sporadic, ALS, only a gene on chromosome 9 has been identified.

The new study, published in *Human Molecular Genetics*, is the result of a large international collaboration led by scientists at the Institute of Psychiatry at King's, in collaboration with universities in the UK, Italy, USA, Germany, Netherlands and France, and is the largest genome wide association study (GWAS) for ALS to date.

A total of 13,225 individuals (6,100 cases and 7,125 controls) were analysed for almost 7 million genetic variants. This included 3,959 newly genotyped Italian individuals (1,982 cases of ALS and 1,977 controls) combined with published genotype data from the Netherlands, USA, UK, Sweden, Belgium, France, Ireland and Italy.

The researchers identified a novel variant on chromosome 17 associated with ALS risk (17q11.2) and confirmed the association with the previously reported gene on chromosome 9 (9p21.2). The association on chromosome 17 was then confirmed in an independent set of 4,656 individuals.

The researchers estimate for the first time that the contribution of common genetic variation to non-familial ALS is approximately 12%. The newly identified genetic variant on chromosome 17 is closely linked to a gene (SARM1) known to play a key role in axon, or nerve fibre death. The authors add that this new finding may lead to the discovery of new pathways involved in ALS, indicating potential new drug targets.

Dr Isabella Fogh and Dr John Powell from the Department of Neuroscience at the Institute of Psychiatry at King's are co-authors of the study.

Dr Fogh says: "This is really exciting work. Whilst there have been a number of genes identified in familial ALS, very few have been identified in sporadic ALS, even though this form of the disease accounts for 90% of cases. Multiple genetic and environmental factors

are implicated in the development of this devastating disorder. What we have here is another key part of the puzzle."

More information: Isabella Fogh et al. 'A genome-wide association meta-analysis identifies a novel locus at 17q11.2 associated with sporadic amyotrophic lateral sclerosis' *Human Molecular Genetics* hmg.oxfordjournals.org/content … /hmg.ddt587.full.pdf

Provided by King's College London